

## SUGAR-CONTAINING AMPHIPHILIC OLIGOMERS

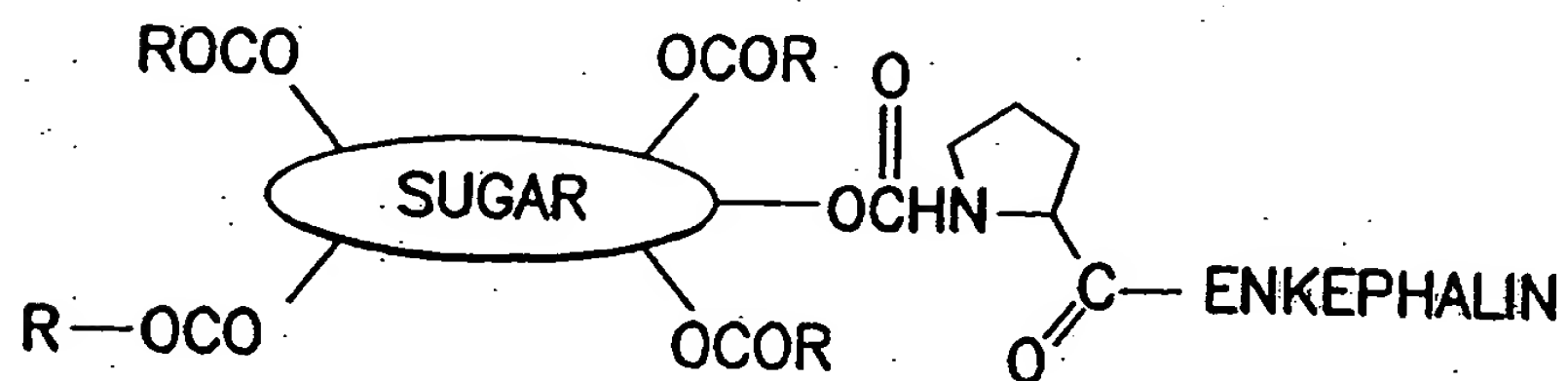


FIG.1A

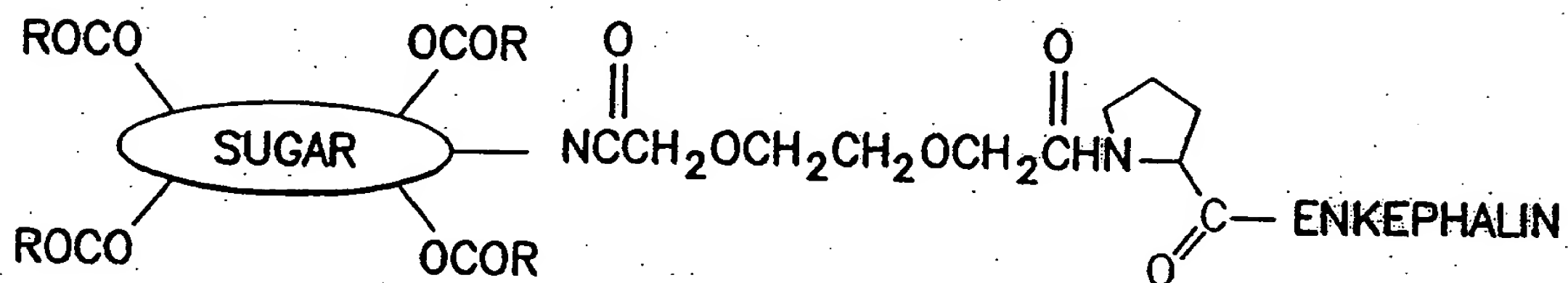


FIG.1B

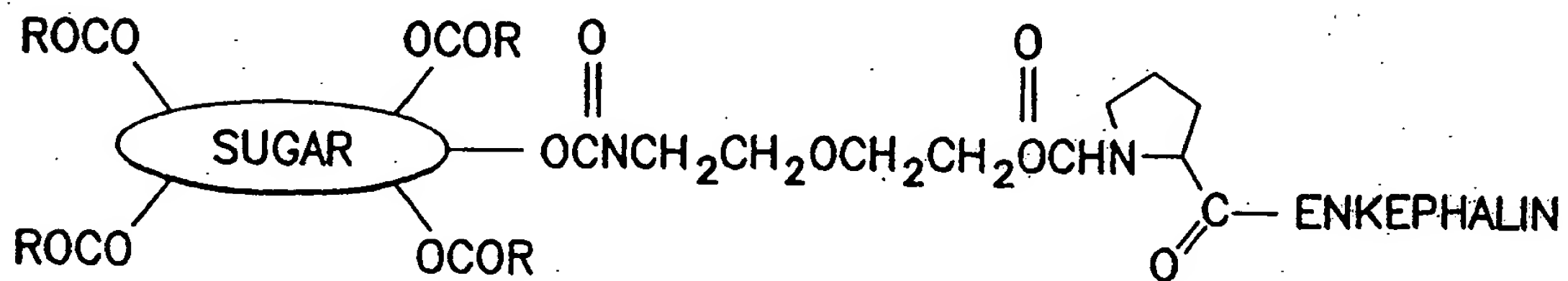


FIG.1C

STABILITY OF ENKEPHALIN AND CETYL-PEG<sub>2</sub>-ENKEPHALIN  
IN RAT BRAIN HOMOGENATE

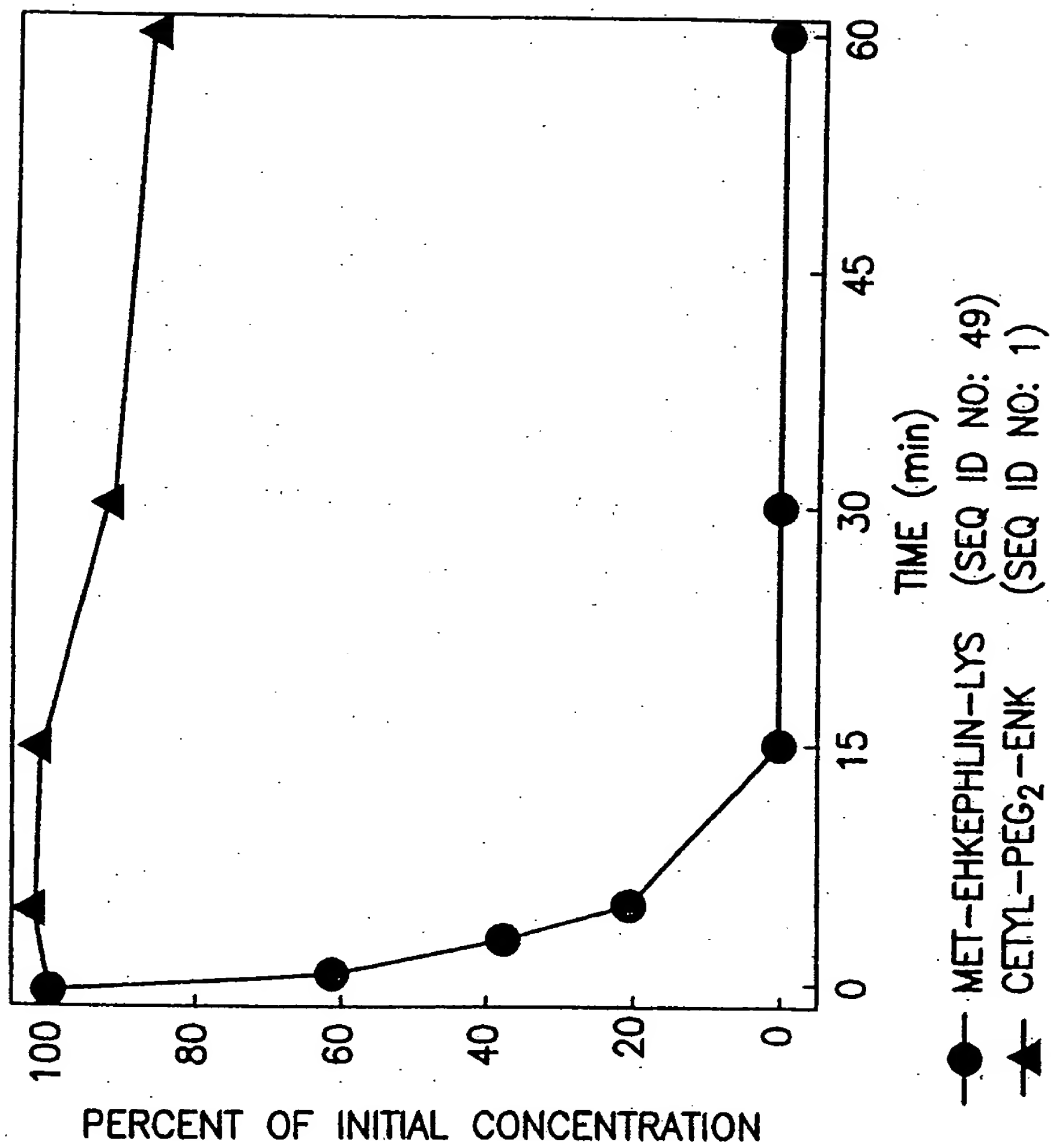


FIG.2

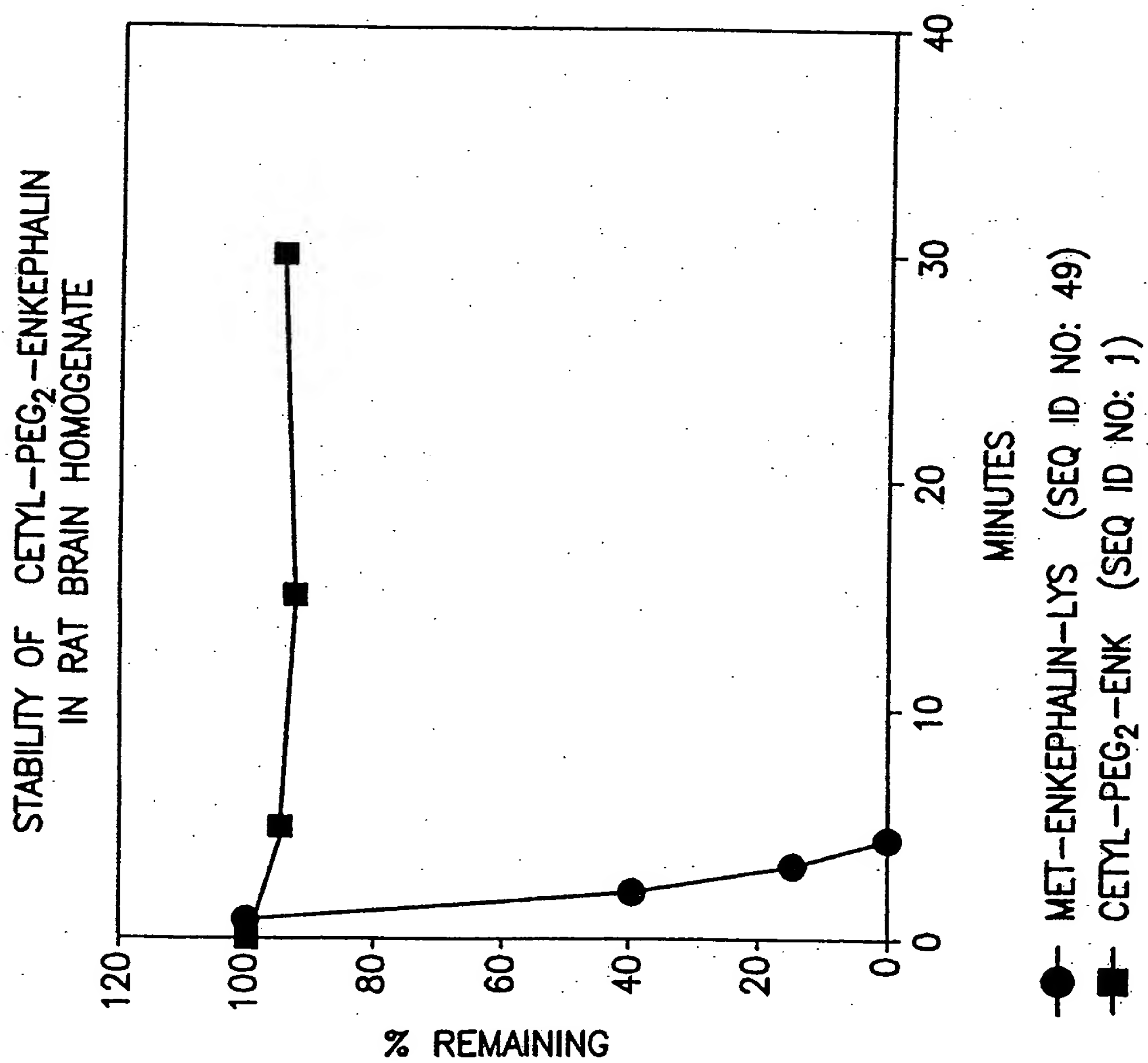


FIG. 3

STABILITY OF PALMITATE-PEG<sub>3</sub>-ENKEPHALIN  
IN RAT BRAIN HOMOGENATE

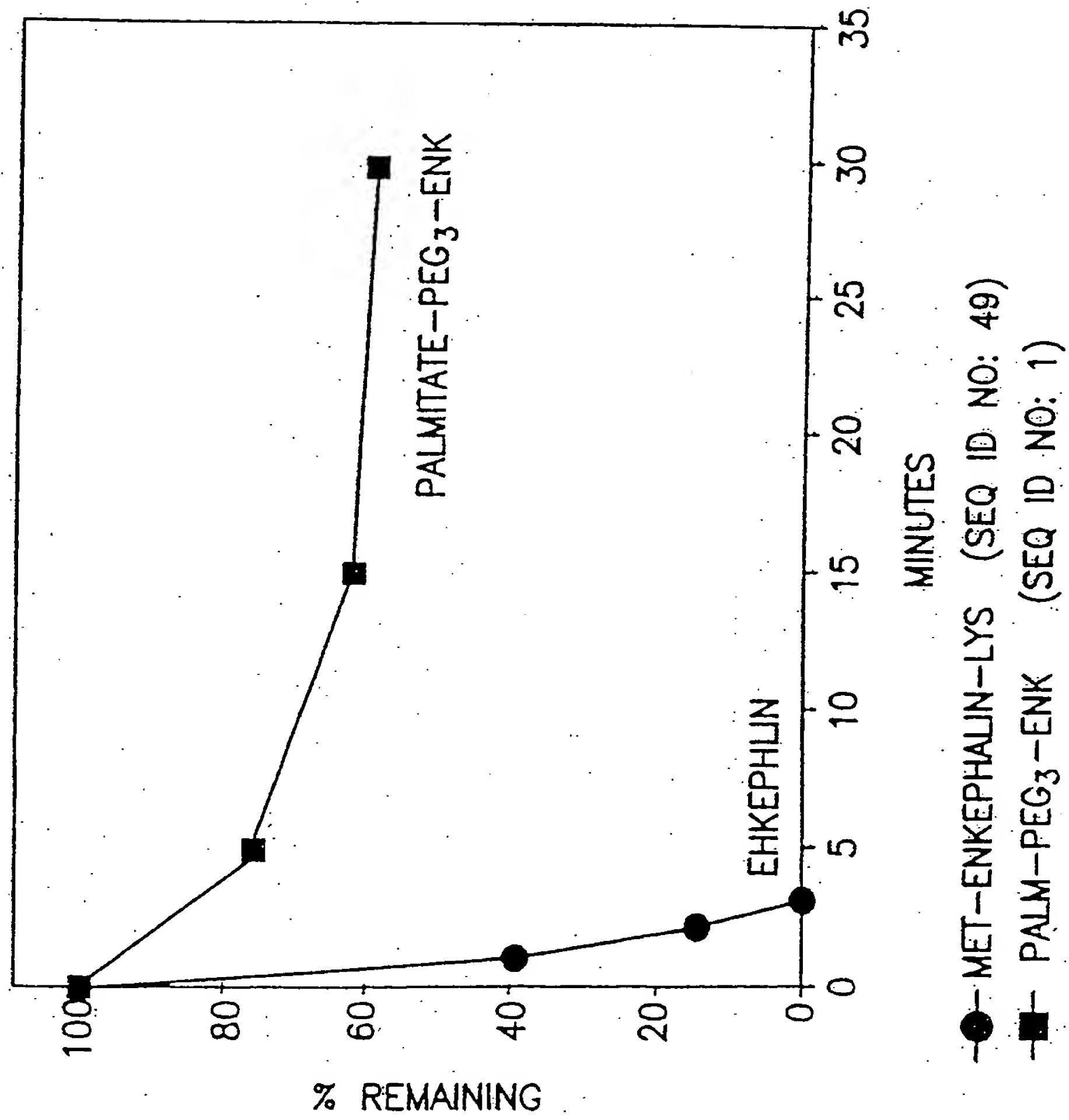


FIG. 4

ISOLATION OF CETYL-PEG<sub>2</sub>-ENKEPHALIN (SEQ ID NO: 1) FROM THE BRAIN

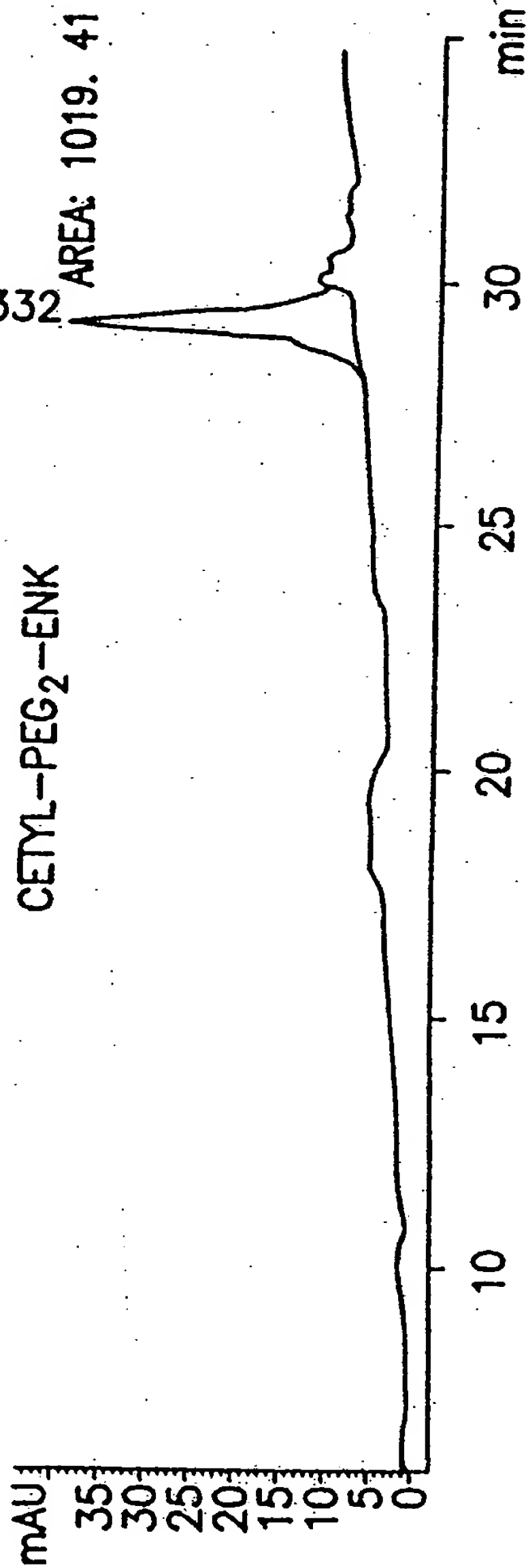


FIG.5A

CETYL-PEG<sub>2</sub>-ENK (SEQ ID NO: 1)

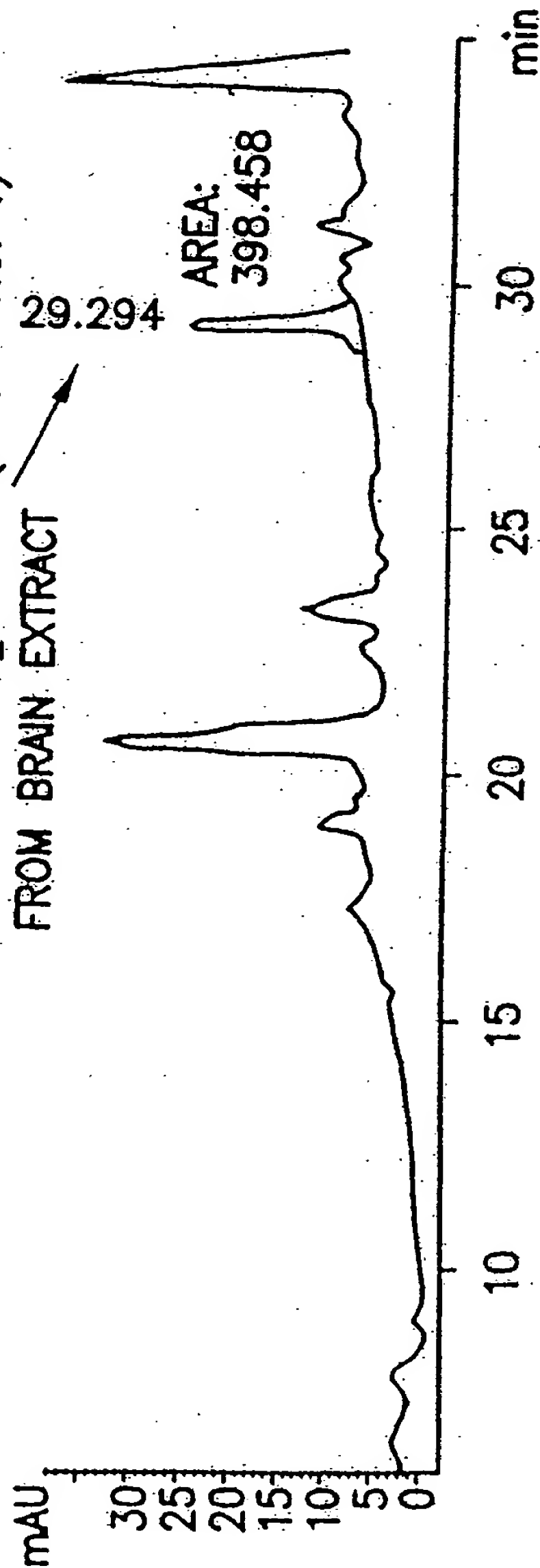


FIG.5B

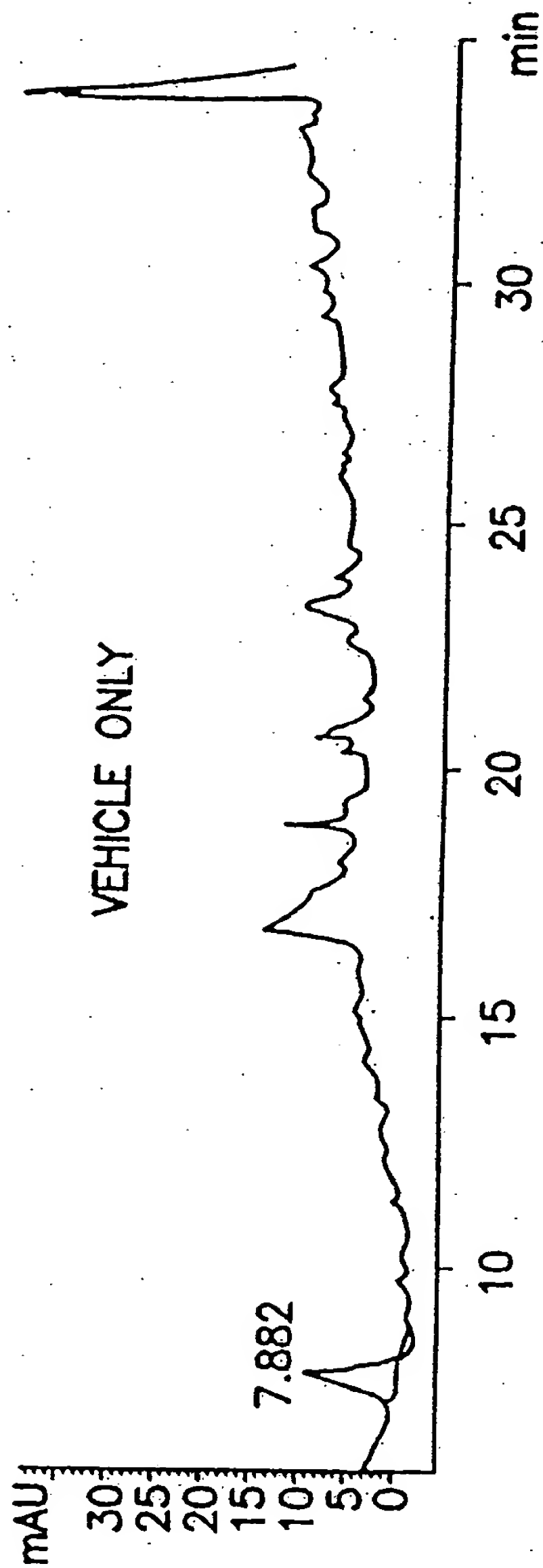


FIG.5C

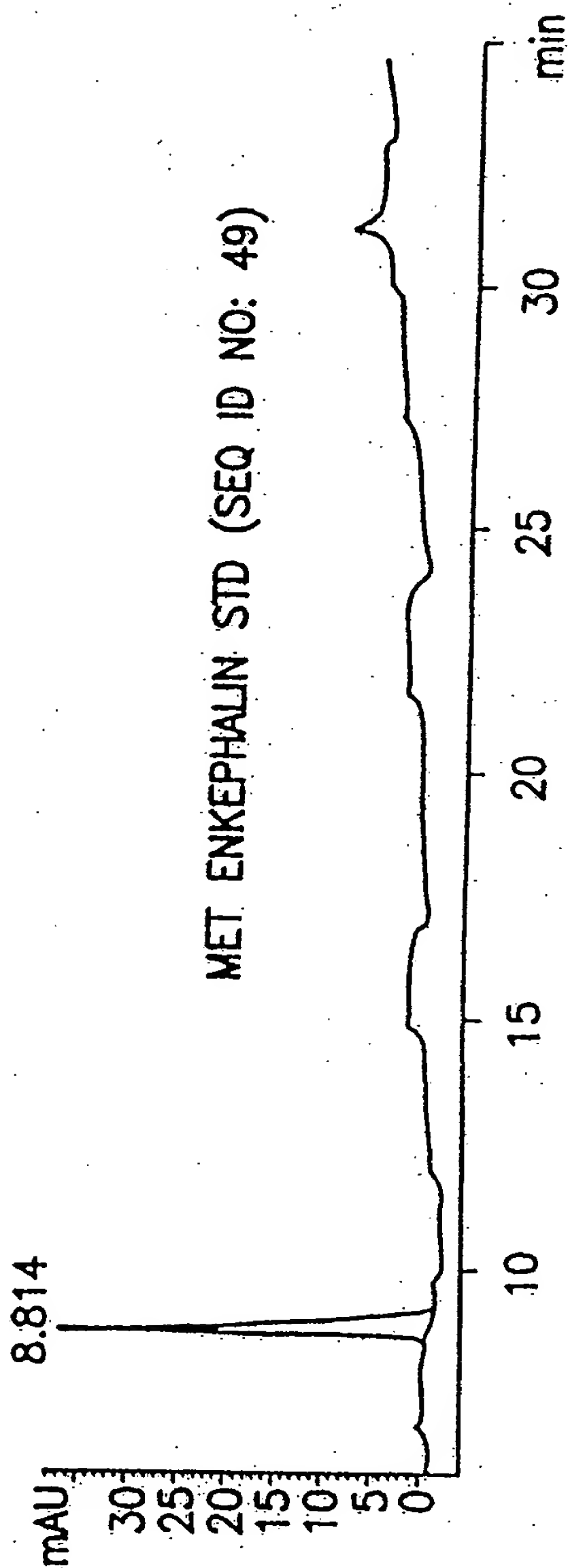


FIG.5D

NALOXONE ANTAGONISM OF  
CETYL-PEG<sub>2</sub>-ENKEPHALIN-INDUCED ANALGESIA

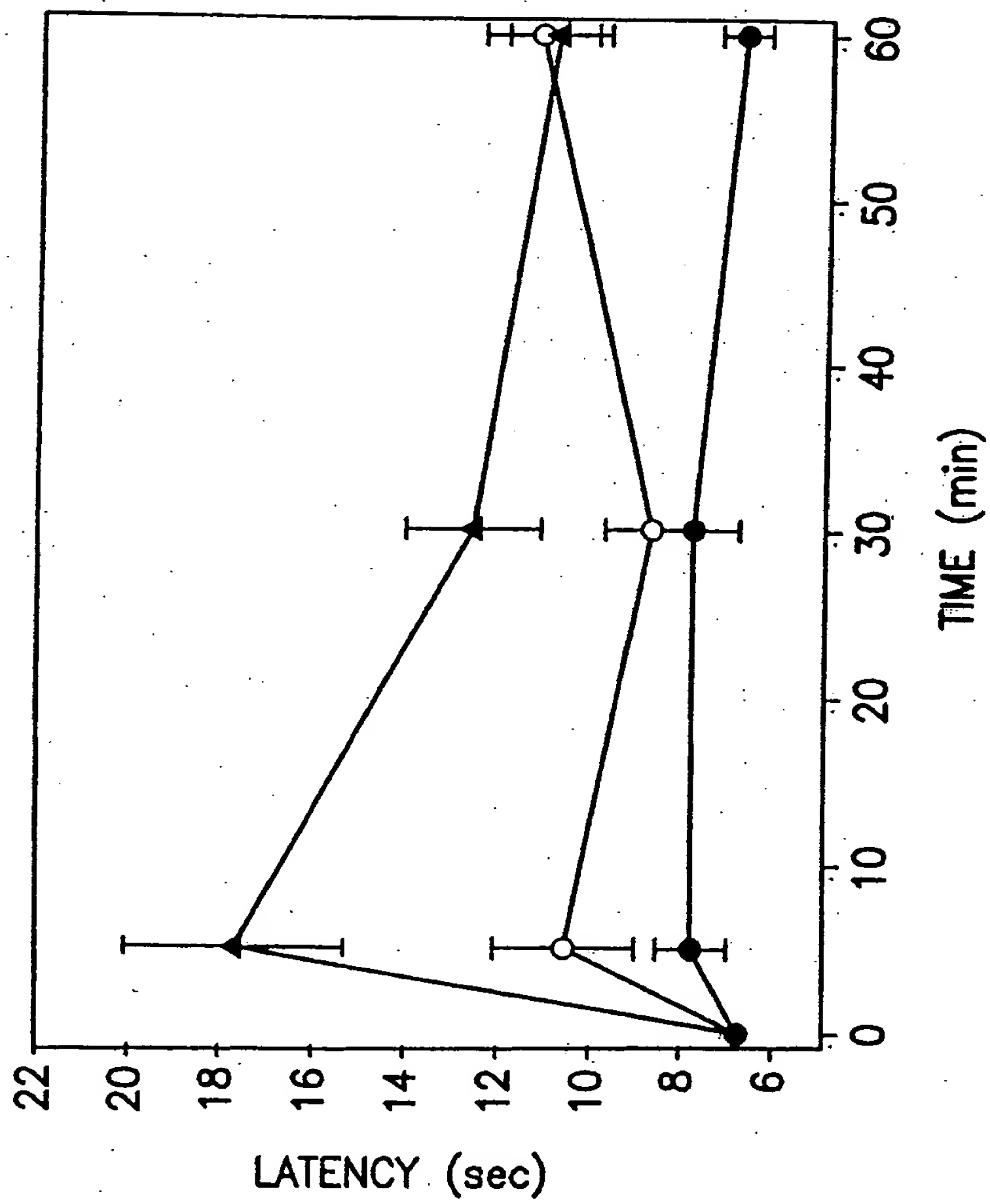


FIG.6

ANALGESIC EFFECT OF A 5 mg/kg IV DOSE OF CETYL-PEG<sub>2</sub>-ENKEPHALIN (SEQ ID NO: 1)  
MONOCONJUGATE IN THE RAT HOT-PLATE ASSAY

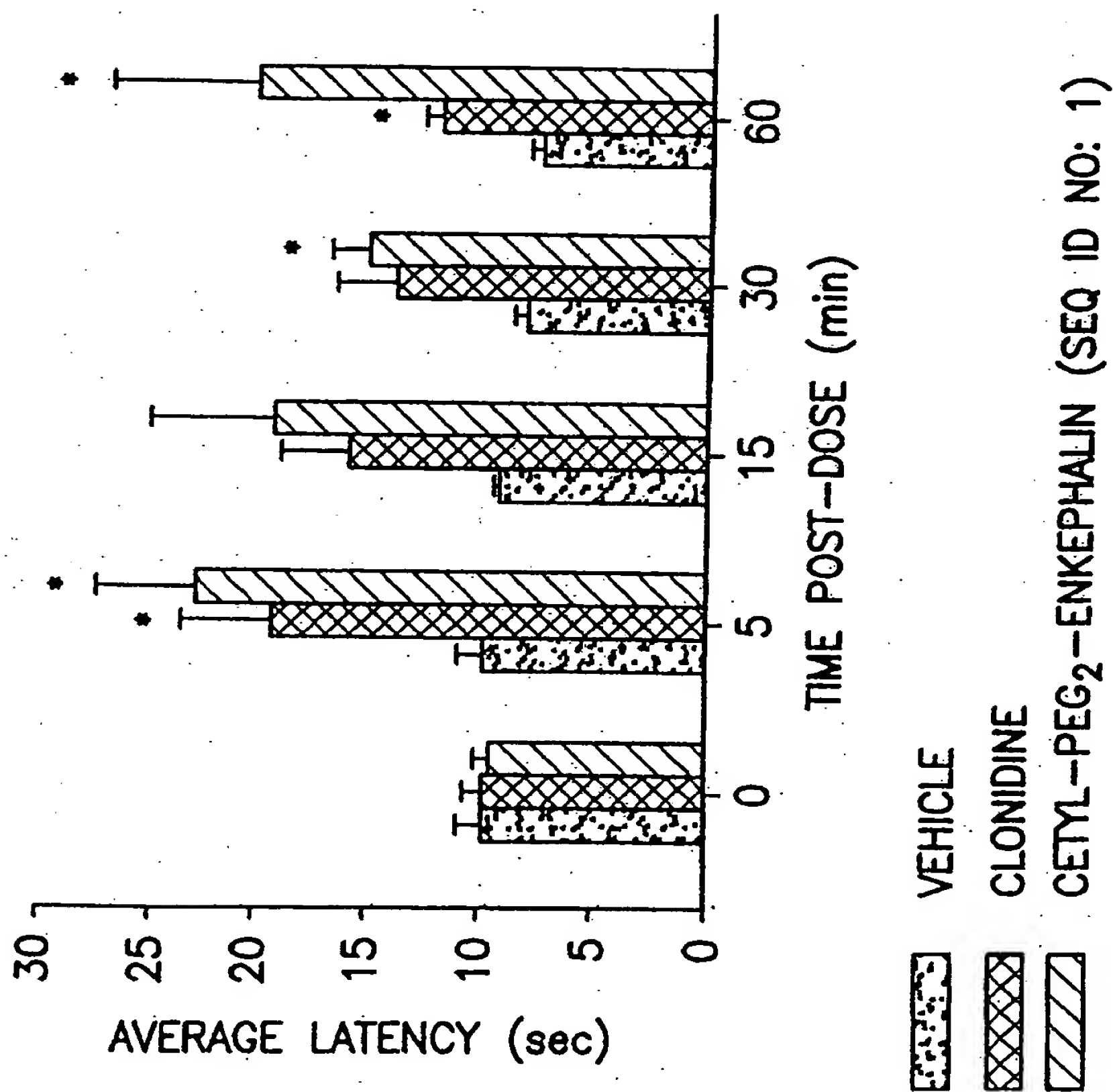


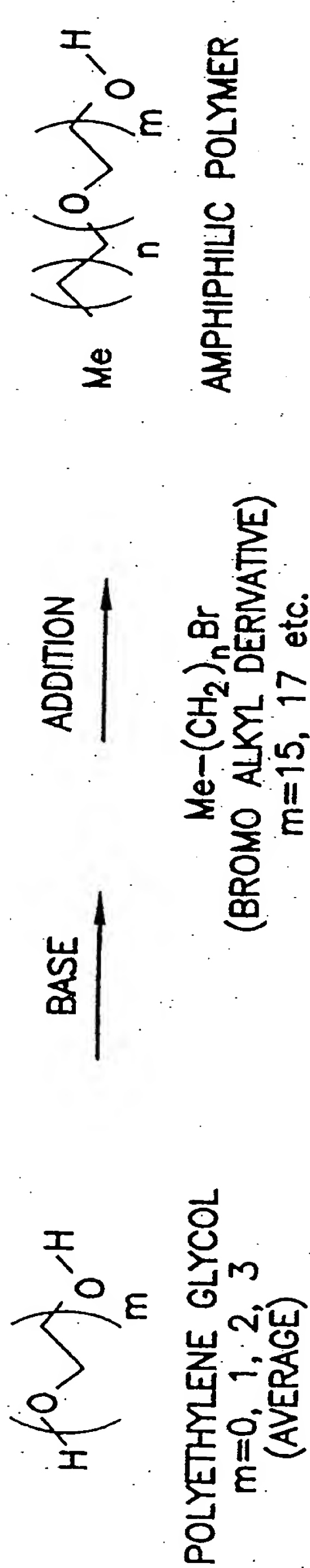
FIG. 7



COMPARISON OF $\mu$ -RECEPTOR BINDING AFFINITY OF ENKEPHALIN CONJUGATES		
DRUG OR CONJUGATE	DETAILED STRUCTURE	% SPECIFIC BINDING
NALOXONE	NALOXONE	100
ENKEPHALIN	MET-ENKEPHALIN-LYS (SEQ ID NO: 49)	67
CETYL-ENK	CETYL-PEG <sub>2</sub> -ENK (SEQ ID NO: 1)	100
CHOL-ENK	CHOLESTEROL-PEG <sub>3</sub> -ENK (SEQ ID NO: 1)	95
DHA-ENK	DHA-PEG <sub>2</sub> -ENK (SEQ ID NO: 1)	63
PALM-ENK	PALMITATE-PEG <sub>3</sub> -ENK (SEQ ID NO: 1)	76
CETYL-TEG-ENK	CETYL-PEG <sub>3</sub> -ENK (SEQ ID NO: 1)	100

FIG.8

# SYNTHESIS OF OLIGOMER



"FREE END"

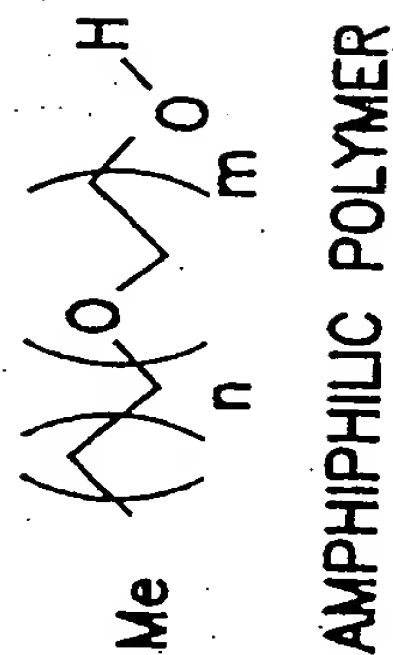
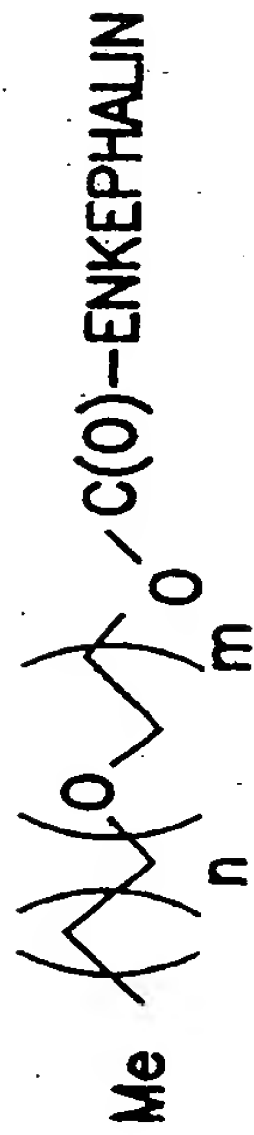
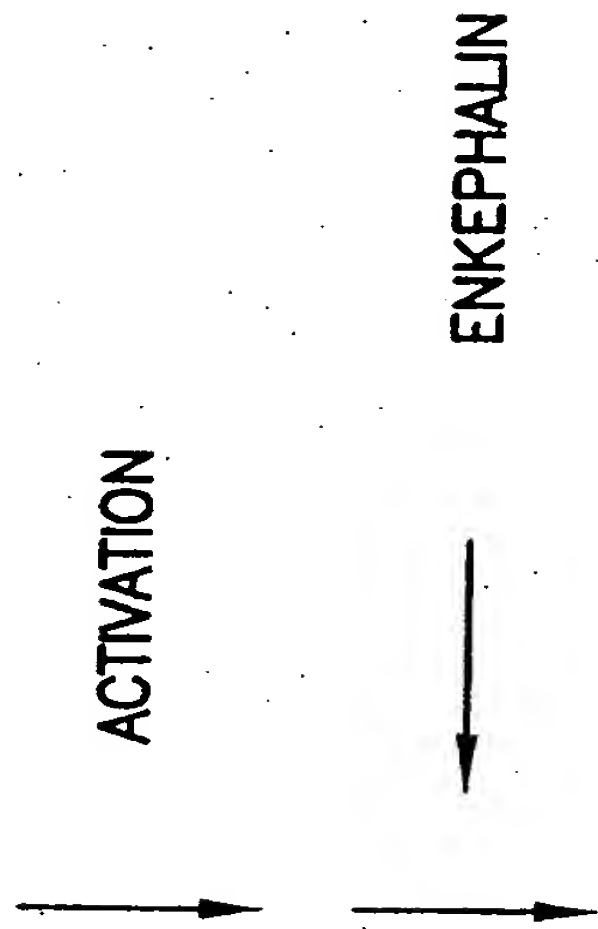
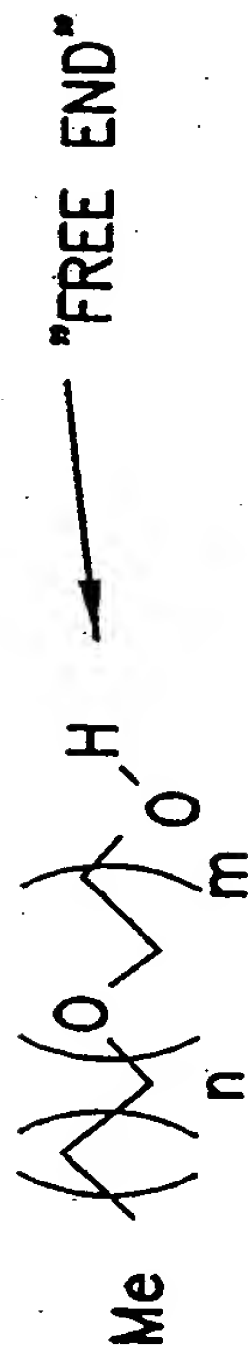


FIG.9

# ATTACHMENT OF OLIGOMER TO ENKEPHALIN



OLIGOMER-ENKEPHALIN-CONJUGATE

EXAMPLE  $m=14$  AND  $n=2$       CETYL-PEG<sub>2</sub>-ENKEPHALIN

FIG.10